VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

Please amend lines 16-17 at page 9 so that they now read:

followed by CAA ($CAG_{9-13}CAA$), (SEQ ID NOs:19-23) with the exception of the 13Q allele which is $CAGCAACAG_{10}CAA$ (SEQ ID NO:18).

IN THE CLAIMS:

Claims 1, 3, 5, 11, 13 and 14 have been amended as follows: Underlines indicate insertions and brackets "[ ]" indicate deletions.

1. (Twice amended) An isolated human hGT1 gene comprising a transcribed polymorphic CAG repeat having the sequence $(CA[U]R)_2(CAG)_nCAA$, wherein [U] R is A or G and n is from 7 to 12, as set forth in SEQ ID NOs:12-17, wherein allelic variants of said CAG repeat are associated with a disorder selected from the group consisting of psychiatric diseases, schizophrenia, affective disorders, neurodevelopmental brain diseases and phenotypic variability with respect to long term response to neuroleptic medication, and wherein n being equal to 11 (SEQ ID NO:16) is the most common allele of the hGT1 gene.

3. (Twice amended) A method for evaluating the severity of schizophrenia of a patient, which comprises the steps of:

a) obtaining a nucleic acid sample of said patient; and

b) determining allelic variants of said CAG repeat of the gene of claim 1,

wherein allelic variants shorter than allele 0, which corresponds to n=11 (SEQ ID NO:16), are indicative of less severe schizophrenia in the patient.

5. (Twice amended) The method of claim 4, wherein said shorter allelic variants have a n equal to 8, 9 or 10 as set forth in SEQ ID NOs:13, 14 or 15.

11. (Amended) The method of claim 10, wherein said sample is a nucleic acid sample and wherein shorter allelic variants have a n equal to 8, 9 or 10, as set forth in SEQ ID NO:13, 14 or 15.

13. (Amended) The human gene of claim 1, wherein n is selected from the group consisting of 7, 8, 9, 10 and 12, as set forth in SEQ ID NOs:12, 13, 14, 15 and 17, and wherein said allelic variant is associated with schizophrenia.

14. (Amended) The human gene of claim 13, wherein n is selected from:

a) n is 7 to 10, as set forth in SEQ ID NOs:12 to 15, wherein said allelic variant is associated with a neuroleptic medication-responsive status of a schizophrenic patient, and

b) n is equal to 12, as set forth in SEQ ID NO:17, wherein said allelic variant is associated with a poor responsive status of a schizophrenic patient to neuroleptic medication.

Serial No. 09/508,821
Supplemental Amendment - Appendix A

Le 16 septembre 1998

Salut France,

Voici les nouveaux infos pour le brevet GT1/schizophrénie. Il y a de la sequence et des infos sur les alleles GT1 déjà mentionné dans le texte initiale.

Amicalement,

Guy Rouleau

The GT1 sequence includes a 5535 bp open-reading frame (ORF) of 5535 bps without interruption showing 85%homology to the mouse cDNA. This ORF is preceeded by a 490 bps intron (including a consensus splice acceptor) and 19 bps of 5'-UTR. The entire ORF may be coded for by a single exon (we are still missing the sequences coding for the last 12 amino acids (36 bp). While this type of genomic organization is very peculiar and not often encountered several lines of evidence suggest that these sequences represent the GT1 gene. First, the presence of a splice acceptor upstream of the ORF suggest that the pre-mRNA will be processed. Second, the chromosomal localisation was determined by polymerase chain reaction (PCR) using the NIGMS somatic cell hybrid panel and two primers designed from our sequences. Sequencing of the previously described hGT1 alleles showed that they code for 10 to 14 glutamines (Q). The CAG-repeat is generally constituted of 9 to 13 CAG repetitions followed by CAA (CAG9-13CAA) with the exception of the 13Q allele which is CAGCAACAG10CAA.

SEQUENCE:

upstream intron is in lowercase; Human gene sequence (exon) is in upper case; the transcription start site ATG in bold. The sequence is from one large (5276 bp) Bam HI fragment and three Pst I fragments (672, 200 and 371 bps)

ggatccagcaggcccaaggggatgagggagcggaaattgctctgctaaatgcttttgagctgtcaggaagg
gctgggagtgatgggtgggggacattggggaggagctggcaatgggcgggggggggcgggtagctcccca
gtgacctggcgctgggcagccggttttgcctcccgcatcagtggccgtccttggcaagactcagctgcagg
cgatgtgggagcgggaattacagagcacacctccctgacacagaagttgtcaatatgcgcacagctggtgg
ggaggctcaggcgaagggggactattaagagctgcgcgggggagcaggcagggtggggaggtgggtggga
gggtgctttctgaggcaaaaggaagtggcccgtctgaatcgctcatcctctgccccctccctgcccatcct
cccctccctccttccctccctccctcccttcctttttcttttcaCAGATAACCAGCCCGAGTC**ATG**CAGTC
TTTTCGAGAAAGGTGTGGTTTCCATGGCAAACAACAGAACTACCAGCAGACCTCGCAGGAAACATCACGCC
TAGAGAATTACAGGCAGCCGAGTCAGGCCGGGCTAAGCTGCGACCGGCAGCGGCTGCTCGCCAAGGACTAT
TATAACCcGCAGCCTTACCCGAGCTATGAGGGTGgCGCTGGCACGCCcTCTGGCACTGCAGCCgCGGTGGC
CGCCGACAAGTACCACCGAGGCAGCAAGGCCCTGCCCACACAGCAAGGCCTGCAGGGGAGGCCGGCTTTCC
CTGGcTACGGCGTCCAGGACAGCAGCCCCTACCCAGGCCGCTATGCTGGTGAGGAGAGCCTTCAGGCTTGG
GGGGCCCCACAGCCACCACCCCCACAGCCGCAGCCACTACCTGCAGGGGTGGCCAAGTATGATGAGAACTT
GATGAAAAAGACAGCAGTGCCCCCCAGCAGGCAGTATGCAGAGCAGGGCGCCCAGGTGCCCTTTCGGACTC
ACTCCCTGCACGTCCAGCAGCCACCGCCGCCCCAGCAGCCCCTGGCATACCCCAAGCTCCAAAGGCAGAAG
CTGCAGAACGACATTGCCTCCCCTCTGCCCTTCCCCCAGGGTACCCACTTTCCTCAGCATTCCCAGTCCTT
CCCCACCTCCTCCACCTACTCCTCCTCTGTCCAGGGTGGTGGGCAGGGGGCCCACTCCTATAAGAGTTGCA
CAGCACCGACTGCCCAGCCCCATGACAGGCCGCTGACTGCCAGCTCCAGCCTGGCCCCGGGGCAGCGGGTC